DOCKET NO.: CACO-0067 (P21303US) PATENT APPLICATION

INT'L. SERIAL NO.: PCT/GB00/00157 INT'L. APPL. FILED: JANUARY 21, 2000

At page 13, replace the paragraph spanning lines 18 - 24 with the following replacement paragraph:

A DNA fragment containing the tac promoter was obtained from plasmid pDR540 (Pharmacia), by PCR amplification using primers 5'- ACCTGACGTCTAAGAAAC -3' (SEQ ID NO:1) and 5'-GCTCTAGATTGTTATCCGCTCAC -3' (SEQ ID NO:2). The amplified DNA fragment was cleaved with restriction endonucleases *Eco*RI and *Xba*I, and the major fragment (369 bp) was cloned between the *Eco*RI and *Xba*I sites of the widely used vector plasmid, pUC19, to generate plasmid pPS1133C2. The sequence of the insert was verified by DNA sequencing (Sanger, *et al.* 1977, Proc. Natl. Acad. Sci. USA, 74: 5463-7).

At page 14, replace the paragraph spanning lines 2 - 7 with the following replacement paragraph:

The two oligonucleotides PS1133A (5'- CTAGGGCCTGCGAGGCCTTAATTAA-GGCCTCCCGGGGCCT -3') (SEQ ID NO:3) and PS1133B (5'-CTAGAGGCCCGGGAGGCCTTAATTAAGGCCTCGCAGGCC -3') (SEQ ID NO:4) were annealed together to generate a short piece of DNA containing two *Sfi*I sites separated by a *Pac*I site, and with 4 nucleotide 5' extensions on either end compatible with ligation into *Xba*I sites. However, only that at the right end regenerates the *Xba*I site:

At page 14, replace the paragraph spanning lines 17 - 20 with the following replacement-paragraph:

The plasmid pET11c (Novagen) was cleaved with XbaI, and the following annealed oligonucleotides were cloned into that site:

PS1134A 5' CTAGAGGCCTGCGAGGC 3' (SEQ ID NO:5) PS1134B 3' TCCGGACGCTCCGGATC 5' (SEQ ID NO:6)

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Replace the paragraph spanning from page 14, line 25 through page 15, line 2 with the following replacement paragraph:

Plasmid pPS1134D4 was cleaved with *Bam*HI, and the following annealed oligonucleotides were cloned into that site:

PS1134C 5' GATCCGGCCTCCCGGGCC

3 ' (SEQ ID NO:7)

PS1134D 3'

GCCGGAGGCCCGGCTAG 5' (SEQ ID NO:8)

At page 15 replace the paragraph spanning lines 14 - 18 with the following replacement paragraph:

DNA sequence derived from the nitroreductase gene (*nfnB*) of *E. coli* strain DH5α was amplified by the polymerase chain reaction from genomic DNA purified from that strain, using primers PS1138A 5'- GGGAATTCCATATGGATATCATTTCTGTCGCCTTAAAGC-3' (SEQ ID NO:9) and

PS1138B 5'- CGCGGATCCTGAGAGGAAATAGCCGGGCAGATGC -3' (SEQ ID NO:10).

At page 17 replace the paragraph spanning lines 17 - 24 with the following replacement paragraph:

The polymerase chain reaction (PCR) was used to determine whether the bacteria in each colony contained $\lambda JG3J1$ or $\lambda JG16C1$. A number of individual colonies were picked at random from the most relevant plates and transferred to a 200 μ l PCR tube, lysed in a microwave for 2min and 35 μ l of PCR reaction mix [16mM (NH₄)₂SO₄, 67mM Tris-Cl (pH 8.8 at 25°C), 0.01% Tween-20 (Bioline), 0.2mM each dNTP, 1.5mM MgCl₂, 1U Biotaq (Bioline)] plus 0.25 μ M primers JG2A 5'-TGGCGGAAAGGTATGCATGC-3' (SEQ ID NO:11) and; JG2B 5'-CAGAGCATTAGCGCAAGGTG-3' (SEQ ID NO:12),

which anneal to λ sequences flanking the *Hin*dIII site, was added.

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